GPI WEB CLIENT

US PAT NO: 5,401,415 [IMAGE AVAILABLE] L9: 3 of 6

SUMMARY:

BSUM(6)

The third method of eliminating **LDL** cholesterol from blood or plasma is adsorption to suitable carrier materials. Thus for example monoclonal and/or polyclonal antibodies which specifically bind the **LDL** cholesterol can be coupled to a porous polyanionic carrier material (J. Clin. **Apheresis** 4, 59-65 (1988), Proc. Natl. Acad. Sci. USA 78, 611-615 (1981), JP 60239425). In addition to antibodies, porous polyanions such. . . 143 369, U.S. Pat. No. 4,096,136, U.S. Pat. No. 4,603,010) have been bound to carrier materials and investigated for specific **LDL** adsorption from plasma or blood. Cellulose, organic polymerisates, coated silica gels and agarose have been described as a carrier matrix. . .

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GPI WEB CLIENT

US PAT NO: 5,424,068 [IMAGE AVAILABLE] L7: 1 of 4

DETDESC:

DETD(4)

The . . . intended (i) to lower the circulating cholesterol level (and, implicitly the LDL circulating level), and this is the case of **lipid** -poor diets and of the **lipid** -lowering drugs and (ii) to counteract the modifications which are considered to make the LDL more atherogenic, which is the case. . . may require a treatment by the two above procedures, but combined with the reducing of circulating cholesterol level by LDL **apheresis** (Scholzek, P. et al. Clinical Investigator, 1992, 70, 99).

5. ☐ Abstract | Bkgnd/Summ | Clms | Draw. Desc | Front | Full | KWIC | Legal | Refs | Cit | Cls

6. 4,895,558, Jan. 23, 1990, Autologous plasma delipidation using a continuous flow system; Bill E. Cham, 604/4; 210/645, 651; 422/44 [IMAGE AVAILABLE]

6. ☑ Abstract | Bkgnd/Summ | Clms | Draw. Desc | Front | Full | KWIC | Legal | Refs | Cit | Cls

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Term	Occurrence
LDL/BI (0P) APHERESIS/BI	6
LDL/BI	1529
APHERESIS/BI	143

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GPI WEB CLIENT

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1. 5,679,260, Oct. 21, 1997, Process for simultaneously removing tumour necrosis factor .alpha. and bacterial lipopolysaccharides from an aqueous liquid; Karl-Siegfried Boos, et al., 210/723, 650, 651, 660, 669, 724, 725, 729, 730, 749, 767, 782; 436/177, 178; 530/412, 414, 415, 416, 417, 418, 419; 604/4, 5 [IMAGE AVAILABLE]

1. ☑ Abstract | Bkgnd/Summ | Clms | Draw. Desc | Front | Full | KWIC | Legal | Refs | Cit | Cls

2. 5,424,068, Jun. 13, 1995, Method for immunization of mammals against atherosclerosis and pharmaceutical compositions for obtaining said immunization; Doina Filip, 424/278.1, 283.1 [IMAGE AVAILABLE]

2. ☐ Abstract | Bkgnd/Summ | Clms | Draw. Desc | Front | Full | KWIC | Legal | Refs | Cit | Cls

3. 5,401,415, Mar. 28, 1995, Adsorption material for the selective removal of LDL and/or vLDL and method of using therefor; Andreas Rauh, et al., 210/660, 198.2, 502.1, 656; 422/70; 436/71, 161; 502/405; 530/413, 417 [IMAGE AVAILABLE]

3. ☑ Abstract | Bkgnd/Summ | Clms | Draw. Desc | Front | Full | KWIC | Legal | Refs | Cit | Cls

4. 5,279,540, Jan. 18, 1994, Method for reducing the risk of atherosclerosis; Michael H. Davidson, 604/4, 5 [IMAGE AVAILABLE]

4. ☑ Abstract | Bkgnd/Summ | Clms | Draw. Desc | Front | Full | KWIC | Legal | Refs | Cit | Cls

5. 5,089,602, Feb. 18, 1992, Process for the manufacture of apolipoproteins from human blood plasma or serum; Henri Isliker, et al., 530/359 [IMAGE AVAILABLE]

GPI WEB CLIENT

US PAT NO: 5,679,260 [IMAGE AVAILABLE] L9: 1 of 6

DETDESC:

DETD(7)

The process according to the invention is substantially analogous to the clinical **apheresis** process described in U.S. Pat. No. 4,908,354, U.S. Pat. No. 4,648,974, EP 0 180 720 and U.S. Pat. No. 4,935,204 (heparin-induced extracorporeal **LDL** precipitation; HELP), which can be used to selectively remove the blood components low density lipoproteins (**LDL**) and fibrinogen from the plasma of patients. The disclosure of these references with regard to possibilities of designing the process.

. .

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GPI WEB CLIENT

US PAT NO: 5,401,415 [IMAGE AVAILABLE] L15: 1 of 3
TITLE: Adsorption material for the selective removal of **LDL** and/or vLDL and method of using therefor

ABSTRACT:

An adsorption material for selectively removing Lp(a) lipoprotein, **LDL** cholesterol and/or vLDL cholesterol from aqueous liquids, in particular from blood, plasma or serum, consisting of porous glass (**beads**), as the solid carrier material whose silanol groups present on its surface carry ligands which are covalently bound and have alkyl residues with 4 to 12 atoms containing at least one ether group and a terminal .alpha.,.beta.-diol group containing alkyl residues with 4 to 12 C atoms and wherein the material has no free silanol groups. Also disclosed is a method of using the adsorption material for selective removal or determination of Lp(a) lipoprotein, **LDL** cholesterol or/and vLDL cholesterol from aqueous liquids, and a device for use in such methods.

SUMMARY:

BSUM(2)

The invention concerns an adsorption material and a process for removing **LDL** cholesterol or/and vLDL cholesterol or/and Lp(a) lipoprotein from aqueous liquids such as plasma or serum, a method for the determination of the concentration of **LDL** cholesterol or/and vLDL cholesterol or/and Lp(a) lipoprotein in liquids as well as a device for the said methods.

SUMMARY:

BSUM(3)

The selective elimination of **LDL** or/and Lp(a) lipoprotein and/or fibrinogen from human blood is desirable for medical reasons in particular for treating a severe familial hypercholesterolaemia and atherosclerosis (Trans. Am. Soc. Artig. Intern. Organs. (1986) 17, 104-107). The familial hypercholesterolaemia is the most dangerous type of hyperlipidaemia. When present in its homozygotic form the affected persons are already in danger of becoming diseased in their youth (and even at a child's age) and dying from severe and rapidly progressing coronary angiopathy (Plasma Sep. and Plasma Frac. 272-280 (Karger Basel, 1983)).

SUMMARY:

BSUM(4)

Previous treatments for severe hypercholesterolaemia have proven to be unsatisfactory. This applies to the various types of diet as well as to

drug therapy. Therefore one has tried to tackle the severe metabolic disorders by means of extracorporeal removal of atherogenic lipoprotein fractions (very low density and low density lipoproteins, vLDL and **LDL**) from blood. The aim of an extracorporeal method of treatment is to achieve a total cholesterol level and **LDL** cholesterol level in the range <200 mg/dl and <130 mg/dl respectively (Klin. Wochenzeitschrift (1987) 69, 161-168; GIT Labor Medizin (1989) 9, 386-395).

SUMMARY:

BSUM(5)

The elimination of **LDL** cholesterol is at present carried out with three different extracorporeal methods. Apart from a cascade filtration (Artherosclerosis 60, 23-37 (1988), Artherosclerosis 73, 197-202 (1988), **LDL** cholesterol can be eliminated by precipitation with heparin in an acidic pH range (HELP method=heparin induced extracorporeal **LDL** precipitation) (Klin. Wochenschrift 65, 161-168 (1987), EP 0 166 324, DE 33 10 727) .

SUMMARY:

BSUM(6)

The third method of eliminating **LDL** cholesterol from blood or plasma is adsorption to suitable carrier materials. Thus for example monoclonal and/or polyclonal antibodies which specifically bind the **LDL** cholesterol can be coupled to a porous polyanionic carrier material (J. Clin. **Apheresis** 4, 59-65 (1988), Proc. Natl. Acad. Sci. USA 78, 611-615 (1981), JP 60239425). In addition to antibodies, porous polyanions such as heparin (DE 36 17 672, U.S. Pat. No. 4,637,944, U.S. Pat. No. 4,103,685) and synthetic oligoanions or polyanions such as sulfated polysaccharides (EP 0 110 409, EP 0 225 867, EP 143 369, U.S. Pat. No. 4,096,136, U.S. Pat. No. 4,603,010) have been bound to carrier materials and investigated for specific **LDL** adsorption from plasma or blood. Cellulose, organic polymerisates, coated silica gels and agarose have been described as a carrier matrix for binding the described substances.

SUMMARY:

BSUM(7)

The results attained up to now with the described adsorption materials are, however, inadequate for the purpose of adsorbing **LDL** to a matrix in an extracorporeal perfusion system in a medical and therapeutic context since either the binding capacity and/or the selectivity of these materials for **LDL** does not meet the practical requirements and/or physiological protective mechanisms (e.g. coagulation system, complement system) are activated. (Artheriosclerosis 73, 143-148 (1988), "Schweiz. med. Wschr." 119, 55-58 . (1989)).

SUMMARY:

BSUM(9)

This object is achieved according to the present invention by an adsorption material for the selective removal of **LDL** cholesterol or/and vLDL cholesterol from aqueous liquids, in particular from blood, plasma or serum, consisting of glass **beads** which have pores as the solid carrier material with organic functional groups as ligands which are covalently bound via silanol groups present on their surface which

is characterized in that it has alkyl residues with 4 to 12 C atoms containing at least one ether group and a terminal .alpha.,.beta.-diol group as the ligands and that no free silanol groups are present.

SUMMARY:

BSUM(10)

The glass **beads** used as a carrier in the adsorption material according to the present invention include glass **beads** , i.e. glass balls of a particular size composed of a silicon dioxide phase with residual amounts of boric acid and alkali oxide, and glass membranes in the form of hollow fibres. Glass **beads** are for example described in DE-A 24 54 111 and in DE 24 62 567. The adsorption material according to the present invention, however, differs from the commercially available variants (Controlled Pore Glass, Nature 206 (1969) 693-696, supplier for example Dow Corning, Electro Nucleonics, Waiko Industries) in that all freely accessible silanol groups have been substituted by organic functional residues. The specific elimination of silanol groups prevents unspecific binding of proteins. Adsorber materials based on pure CPG (Controlled Pore Glass) with completely or partially intact silanol groups exhibit undesired HDL binding properties (see example 1). In contrast it surprisingly turned out that the adsorption materials substituted according to the present invention in which all of the silanol groups are substituted, of which at least one position is substituted by an ether group which may be followed by a terminal .alpha.,.beta.-diol group, are able to bind **LDL** cholesterol and vLDL cholesterol and Lp(a) lipoprotein with a previously unachievable kinetic reaction, selectivity and binding capacity.

SUMMARY:

BSUM(24)

The pore diameter of the glass **beads** in the adsorption material according to the present invention is larger than that of the **LDL** cholesterol and vLDL cholesterol molecules which are to be adsorbed, thus it is more than 30 nm.

SUMMARY:

BSUM(25)

It is preferred that the glass **beads** used have a particle diameter of 60 to 250 .mu.m and a pore diameter of 50 to 150 nm.

SUMMARY:

BSUM(26)

The invention also concerns a process for the production of an adsorption material according to the present invention in which the desired ligands are coupled by means of a silylation reaction to the SiOH groups of the glass **beads** via a disiloxane bond -Si-O-Si-L in which L denotes the ligands. This silylation reaction is described by Shung et l. (J. of Chrom. 120 (1976) 321-333). Starting materials which can be used according to the present invention are supplied by the manufacturers Schott, Mainz FRG; Dow Corning, Electro Nucleonics and Waiko Industries among others and are referred to as Bioran glass carrier materials or Controlled Pore Glass (CPG) carriers. In a preferred embodiment of the invention .gamma.-glycidoxypropyltri-methoxysilane and a silanol-Bioran carrier in

the form of glass **beads** are used for the silylation reaction and glycidoxypropyl-Bioran-disiloxane is obtained and this product is subjected to an acidic treatment during which the epoxide residue opens to yield the particularly preferred ligand according to the present invention the 1,2-dihydroxypropyl-3-oxypropyl residue, which is bound as a disiloxane group.

SUMMARY:

BSUM(28)

The adsorption materials synthesized and used according to the invention exhibit excellent properties in that they selectively and quantitatively bind **LDL** cholesterol and vLDL cholesterol and also Lp(a) lipoprotein without at the same time eliminating HDL cholesterol.

SUMMARY:

BSUM(29)

The invention also concerns a process for removing **LDL** cholesterol or/and vLDL cholesterol from aqueous liquids, in particular blood, plasma or serum in which the liquid is passed over an adsorption material according to the present invention. A further application of the adsorption material according to the present invention and thus a further subject matter of the invention is a method for the determination of the concentration of **LDL** cholesterol or/and vLDL cholesterol in aqueous liquids, in particular blood, plasma or serum which is characterized in that **LDL** cholesterol and vLDL cholesterol are separated chromatographically from the liquid with the aid of an adsorption material according to the present invention and after elution from the adsorption material their concentration is determined according to known methods. In this connection it is preferred that the elution is carried out with high molecular saline solution, a glycerol-water mixture or a urea solution (example 10).

SUMMARY:

BSUM(30)

A characteristic of the materials according to the present invention compared to comparable materials is that they bind **LDL** and vLDL with a kinetic reaction, selectivity and binding capacity (>20 mg **LDL** per ml adsorbent) which was hitherto unachievable, that they eliminate these components not only from plasma or serum but also directly from stabilized whole blood with high efficiency and that they do not activate any physiological protective mechanisms (e.g. coagulation system, complement system) by unspecific adsorption of the corresponding components (example 10 and 11).

SUMMARY:

BSUM(31)

Furthermore the invention provides a device for the extracorporeal removal of **LDL** cholesterol or/and vLDL cholesterol from aqueous liquids, in particular from blood, plasma or serum, wherein this device is composed of a cylindrical housing which is filled with an adsorption material according to the present invention and the ends of which are provided with covers which each have central inflow or outflow pipes. This cylindrical housing preferably has a diameter of 3 to 20 cm, preferably of 5 to 10 cm and a length of 1 to 40 cm, preferably of 10 to

20 cm. The preferred material for the housing is glass or plastic (example 10 and 11).

SUMMARY:

BSUM(32)

In a further preferred embodiment of the device according to the present invention the cover on the inflow side of the housing has a sieve with a pore size of 10 to 300 .mu.m, preferably 20 to 100 .mu.m. This prevents blockage of the device by larger particles present in the aqueous liquid. The device according to the present invention can be sterilized in a packaging by means of .gamma.-radiation or by heat and is thus particularly suitable for use in an extracorporeal perfusion system. It can, however, also be used practically as a chromatography column, in particular in order to determine the **LDL** cholesterol and/or vLDL cholesterol concentration according to the present invention.

SUMMARY:

BSUM(33)

In a particularly preferred embodiment of the invention the housing of the device is integrated in a closed circuit in which the aqueous liquid is circulated by means of a pump. It is particularly preferable to equip the device with two cylindrical housings (two adsorption capsules) which can be alternately turned on by means of valves and which can be rinsed with the aqueous liquid which is to be treated in a closed circuit by means of a pump. The capsule which has not been rinsed and is saturated with **LDL** or vLDL is eluted with a regeneration solution which is preferably a high molecular saline solution, glycerol-water mixture or a urea solution.

DETDESC:

DETD(9)

The eluates 2, 3, 4, 5 and 6 ml were used as assessment parameters for the kinetic time courses of adsorption capacity. The intermediate eluates combined in the mixture were examined as a selectivity "screening criterium" for the selectivity of individual synthesized adsorber material. Total cholesterol, HDL, **LDL** and protein content was determined in the eluates (cholesterol oxidase PAP test, cholesterol oxidase iodide test and biuret test).

DETDESC:

DETD(10)

TABLE 1

CPG 500 (with free silanol groups)

Initial plasma (mg/dl)	Mixture of the intermediate eluates (mg/dl)	Adsorption capacity (%)

Total cholesterol		
217	147	32
HDL cholesterol		
41	7	83
LDL cholesterol		
153	119	22
Total protein		
7	6.3	10

DETDESC:

DETD(12)

As shown by Table 1, native CPG 500 glass with non-reacted silanol groups is capable of binding total cholesterol. Since, however, the HDL cholesterol is quantitatively eliminated this qualifies the **LDL** binding capacity. The elimination of HDL cholesterol has to be regarded as a major disadvantage.

DETDESC:

DETD(15)

Test of the total cholesterol adsorption capacity of glass **beads** coated with 1-aminoethyl-3-oxybutyl groups or alternatively with 1-hydroxyethyl-3-oxybutyl-/glycidopropyl groups (ratio 1:1) (manufacturer's name NH.sub.2 - and -OH/epoxide-hydrophilic Bioran glass, Schott Co. Mainz) 100/130/250, the pore size depending on the species is 100-200 nm, the particle size is 60-280 .mu.m).

DETDESC:

DETD(19)

The binding capacities for total cholesterol shown in Table 2 is relatively high for the Bioran glass **beads** substituted with NH.sub.2 groups, however, this species quantitatively absorbs the-HDL cholesterol (data not shown). For these reasons the "glass **beads** " modified with NH.sub.2 can only be used for reactions with various ligands.

DETDESC:

DETD(22)

Immobilization of organic functional groups on Bioran "glass **beads** " and a test for the adsorption capacity of the synthetic adsorption materials.

DETDESC:

DETD(24)

"Glass **beads** " were used as the starting material for the immobilization reaction analogous to example 2 (Schott Co. pore size, particle size see example 2), these are reacted with sulphuric acid. The epoxide group is opened in this process to form in each case a 1,2-dihydroxypropyl-3-oxypropyl group.

DETDESC:

DETD(25)

6 g in each case of wet Bioran 100, 130 and 250 glass **beads** (see example 2) with -CH.sub.2 OH groups and epoxide groups (ratio 1:1) is shaken (100 rpm) for 3 days at 40.degree. C. with 1N H.sub.2 SO.sub.4. The adsorbent is subsequently washed with 10 parts by volume distilled water on a G3 filter and taken up in the respective equilibration buffer.

DETDESC:

DETD(28)

TABLE 3

Total cholesterol determination of synthetic products derived from Bioran "glass **beads** "

	Initial plasma (mg/ml)	Mixture of the intermediate eluates (mg/ml)	Adsorption capacity (%)
1,2-dihydroxypropyl-3-oxypropyl-Bioran-disiloxane 100	217	126	42
1,2-dihydroxypropyl-3-oxypropyl-Bioran-disiloxane	217	93	57

130

1,2-dihydroxypro-

217 97 55

pyl-3-oxypropyl-

Bioran-disiloxane

250

DETDESC:

DETD(30)

All Bioran "glass **beads** " covered with the functional group according to the present invention have excellent binding properties. Unlike the NH.sub.2 -Bioran modified "glass **beads** " and the CPG 500 glass (see examples 1 and 4), the materials are not able to bind HDL.

DETDESC:

DETD(34)

TABLE 4

1-hydroxyethyl-3-oxybutyl/1,2-dihydroxy-3-

oxypropyl/1,1-dimethoxyethyl-2-oxypropyl-Bioran-

disiloxane (ratio 1:1.3:0.8) 100

	Initial plasma (mg/ml)	Mixture of the intermediate eluates (mg/ml)	Adsorption capacity (%)
Total cholesterol	217	126	42
LDL cholesterol	153	66.6	56.5
HDL cholesterol	41	41	--
Triglycerides			

117	92	21.4
Total protein		
7 (g/dl)	6.9 (g/dl)	1.5

DETDESC:

DETD(35)

TABLE 5

1-hydroxyethyl-3-oxybutyl/1,2-dihydroxy-3-oxypropyl/1,1-dimethoxyethyl-2-oxypropyl-Bioran-disiloxane (ratio 1:1.3:0.8) 130

Initial plasma (mg/ml)	Mixture of the intermediate eluates (mg/ml)	Adsorption capacity (%)
Total cholesterol		
217	93	57
LDL cholesterol		
153	38.4	75
HDL cholesterol		
41	39	4.9
Triglycerides		
117	78	33.3
Total protein		
7 (g/dl)	6.7 (g/dl)	4.2

DETDESC:

DETD(36)

The adsorption materials described in example 4 exhibit a high

selectivity and adsorption capacity for **LDL** cholesterol. Neither HDL cholesterol nor total protein is bound by the adsorption material. None of the kinetic experiments shows a saturation of the material after passage of 6 ml plasma.

DETDESC:

DETD(38)

Test of the adsorption selectivity and capacity of "glass **beads** " with 1-hydroxyethyl-3-oxybutyl-/1,2-dihydroxy-3-oxypropyl-Bioran-disiloxane using whole blood.

DETDESC:

DETD(47)

Synthesis of porous "glass **beads** " and test for the adsorption capacity of the synthesized adsorber species using human plasma.

DETDESC:

DETD(50)

6 g wet glycidoxy-3-propyl-3-Bioran-disiloxane 100 "glass **beads** " were shaken for 3 days at 40.degree. C. with 1N H.sub.2 SO.sub.4 (100 rpm). The adsorbent was subsequently washed in a G3 filter with 10 parts by volume distilled water and taken up in equilibration buffer.

DETDESC:

DETD(53)

TABLE 7

Human plasma passed over the adsorber material

1,2-dihydroxypropyl-3-oxypropyl-Bioran-disiloxane

Initial plasma (mg/ml)	Mixture of the intermediate eluates (mg/ml)	Adsorption capacity (%)
Total cholesterol		
225	120	46.6
LDL cholesterol		
152	58	61.8
HDL cholesterol		
33	33	--

Triglycerides

115 89 22.6

DETDESC:

DETD(56)

Clinical-biochemical routine diagnostics of human plasma fractions passed over porous "glass **beads** ".

DETDESC:

DETD(58)

Adsorption material (Bioran "glass **beads** " pore size 120 nm, particle size 130 .mu.m analogous to example 2) was synthesized analogous to example 3 and coated with organic functional spacer arms comprising 1,2-dihydroxypropyl-3-oxypropyl residues, 1-hydroxyethyl-3-oxypropyl residues and 1,1-dimethoxyethyl-2-oxypropyl residues in a ratio of 1:1.3:0.8 and tested in a plasma experiment.

DETDESC:

DETD(61)

TABLE 8

	Column fraction					
	I	2	3	4	5	6
Sodium mmol/l	143	127	135	139	142	142
Potassium mmol/l	4.0	3.0	3.6	3.8	3.9	3.9
Calcium mg/dl	9.5	8.6	8.9	8.8	9.4	9.1
in.phosphorus mg/dl	3.2	3.0	3.0	3.2	3.1	3.4
Chloride mmol/l	102	96	100	101	102	102
Creatinine mg/dl	1.0	0.9	0.9	1.0	1.0	0.9
Urea-N mg/dl						

	14	13	14	14	14	15
Glucose mg/dl						
	98	88	90	91	94	94
Total protein g/dl						
	6.9	6.4	6.5	6.6	6.7	7.0
Albumin g/dl						
	4.5	4.3	4.3	4.4	4.3	4.4
Total bilirubin mg/dl						
	0.4	0.4	0.4	0.4	0.4	0.4
LDH U/l	136	132	128	128	129	136
Amylase U/l						
	21	21	20	20	21	21
Iron .mu.g/dl						
	100	88	87	87	87	89
IgG g/l	12.8					
		12.3	12.4	12.3	12.6	12.7
IgA g/l	2.5	2.4	2.4	2.4	2.4	2.5
Igm	1.7	1.5	1.5	1.5	1.6	1.6
C-3 compl. %						
	59	51	49	48	51	53
C-4 compl	21	20	19	19	20	21
C-1 inact. %						
	28	11	21	24	22	21
AT III %	111	104	102	107	101	102
Haemoglobin mg/dl						
	13	10	10	9	10	11
Heparin iu/ml						
	8.25					
		6.4	6.9	6.6	6.55	6.85
Tot. chol. mg/dl						
	196	56	62	62	67	83
Tot. TG. mg/dl						

69 20 26 32 37 44

LDL chol. mg/dl

121 0 0 0 0 11

HDL chol. mg/dl

68 56 62 62 62 66

Apo A 1 mg/dl

156 146 151 152 150 160

Apo B mg/dl

106 <20 <20 <20 <20 <20

Lp(a) mg/dl

24.5

1.85 2.0 2.65 4.1 6.6

Fibrinogen mg/dl

272 258 231 231 231 258

Plasminogen mg/dl

18.4

12.6 17.6 18.4 18.4 19.2

I = initial value

2-6 = column fraction (in ml)

DETDESC:

DETD(72)

The spectra determined for the compounds A/B/C are shown in FIG. 1. All three compounds differ in their signals. Only the signal peak at 21.8 occurs in all the samples. It represents the -C-C-C-O backbone. This is the primary function which is the basis for all residues (A/B/C). Only the adsorption material (sample C) synthesized according to example 3 fulfils the required quality criteria in relation to its **LDL** binding capacity. The solid-state NMR spectrum documented under C can be used as a quality criterium for the adsorption material.

DETDESC:

DETD(74)

Test for the total cholesterol adsorption capacity of glass **beads** covered with 1-hydroxyethyl-3-oxybutyl/glycidoxypropyl groups (manufacturer's name -OH/epoxide hydrophilic Bioran glass, Schott Co., Mainz), pore size 100-120 nm depending on the species, particle size 60-280 .mu.m.

DETDESC:

DETD(81)

After 2 ml of pre-eluate, 10 eluates of 1 ml are obtained of which the total cholesterol content, HDL content and **LDL** content is determined in comparison to the initial concentration (cholesterol oxidase PAP, cholesterol oxidase iodide test).

DETDESC:

DETD(82)

The adsorption capacity is determined by integrating the areas of the amounts of adsorbed total cholesterol, **LDL** cholesterol and HDL cholesterol.

DETDESC:

DETD(83)

TABLE 9

Total cholesterol	**LDL** cholesterol	HDL cholesterol						
abso-								
adsor-	abso							
	adsor-	abso-						
		adsor-						
lute								
bed	lute							
	bed	lute						
		bed						
(mg)								
(mg)								
	(%)							
		(mg)						
			(mg)					
				(%)	(mg)			
						(mg)		
							(%)	

1-hydroxyethyl-

45.6

20 43.8

30.4

10 32.9

9.6

0.8 7.8

3-oxybutyl/

1,2-dihydroxy-

propyl-3-oxy-

propyl-Bioran-

disiloxane 100

(ratio 1:4)

1-hydroxyethyl-

45.6

16.6

36.4

30.4

15.1

49.8

9.6

-- --

3-oxybutyl/

1,2-dihydroxy-

propyl-3-oxy-

propyl-Bioran-

disiloxane 100

(ratio 1:1)

1-hydroxyethyl-

45.6

13.4

29.3

30.4

13.9

45.8

9.6

-- --

3-oxybutyl/

1,2-dihydroxy-

propyl-3-oxy-

propyl-Bioran-

disiloxane 100

(ratio 3:1)

DETDESC:

DETD(85)

The results show that the binding capacities of the adsorbed amounts of cholesterol depend on the ratio of the 1-hydroxyethyl-3-oxybutyl/1,2-dihydroxypropyl-3-oxypropyl composition. The sample having the reaction ratio (1:1) has the largest capacitiy for **LDL** cholesterol without binding additional HDL cholesterol.

DETDESC:

DETD(87)

This additional HDL cholesterol binding property is not observed in the sample having the reaction ratio of (1:3) but in this case the total cholesterol capacity is reduced and thus also the **LDL** cholesterol binding capacity.

DETDESC:

DETD(88)

The largest adsorption capacity with corresponding **LDL** cholesterol selectivity is achieved using the reaction ratio of (1:1).

DETDESC:

DETD(90)

Synthesis of porous "glass **beads** " and test for the adsorption capacity of the synthesized adsorber species with whole blood and subsequent regeneration.

DETDESC:

DETD(91)

Synthesis of porous glass **beads**

DETDESC:

DETD(93)

The 1-hydroxyethyl-3-oxypropyl/glycidoxypropyl-Trisola-disiloxane 200 (ratio 3:1) "glass **beads** " are washed with distilled water after the treatment with 1N H.sub.2 SO.sub.4 and equilibrated with physiological phosphate buffer (pH 7.4, 20 mmol/l PO.sub.4.sup.3 -).

DETDESC:

DETD(99)

The adsorption capacities with respect to total cholesterol and **LDL** cholesterol of the 1st and 2nd run are compared as a criterium for evaluating the ability to regenerate the adsorbent. In addition all relevant clinical-biochemical diagnostic parameters (including urea determination) of the whole blood fractions which have passed through the adsorption material are tested (20 ml eluates).

DETDESC:

DETD(100)

TABLE 10

Cholesterol adsorption of Trisola glass **beads**

	Total cholesterol pool c (mg/dl)	adsorbed total absolute in cholesterol in the blood 80 ml whole blood c (mg)	absolute from 80 ml whole blood c (mg)	(%)
1st run				
before regenera-tion	275	220	108	49.27
2nd run				
after	275	220	109	49.86

regenera-

tion

LDL cholesterol adsorbed

absolute in **LDL** cholesterol

in the blood

80 ml whole absolute from 80 ml

pool blood whole blood

c (mg/dl) c (mg) c (mg) (%)

1st run

175 140 99 69.29

before

regenera-

tion

2nd run

175 140 101 72.14

after

regenera-

tion

DETDESC:

DETD(104)

Clinical-biochemical routine diagnostics of whole blood fractions and of whole blood fractions passed over "glass **beads** ".

DETDESC:

DETD(112)

TABLE 11

Data in ml 1

Concen-

Initial

tration

value

		100-200					
			140-160				
				180-200			
					260-280		
						320-340	
							300-400
Sodium mmol/l							
	143	145	143	143	142	142	141
Chloride							
mmol/l							
	98	101	98	90	99	99	99
Tot. protein							
g/dl	1.2	6.5	7.2	6.9	6.9	7.3	7.2
Tot. chol.							
mg/dl							
	193	43	59	65	78	94	105
Triglycerides							
mg/dl							
	101	41	53	50	64	70	80
HDL-Chol.							
mg/dl							
	49	38	48	50	48	51	49
LDL -Chol.							
mg/dl							
	124	0	0	3	17	29	56
IgG mg/dl							
	10.8						
		10	11.3	11.2	11.1	10.6	11.1
IgA mg/dl							
	2.3	2.2	2.5	2.4	2.4	2.4	2.4
IgM mg/dl							

	2	1.7	2.1	2	2	2.1	2
C-1 Compl.							
mg/dl							
	29	19	23	25	25	24	26
C-3 Compl.							
mg/dl							
	61	53	64	64	64	61	59
C-4 Compl.							
mg/dl							
	21	18	20	20	21	20	20
Fibrinogen							
mg/dl							
	109	109	107	110	107	106	108
AT III %	11.1						
	11	11.2	11.9	11.3	12.2	11	
Plasminogen							
%	13.2						
	10.6	11.2	11.8	11.8	11.2	11.8	
Lp (a) mg/dl							
	75	4.5	9	12.3	23	31.4	39.8
Apo Al mg/dl							
	172	122	172	176	179	178	183
Apo B mg/dl							
	78.8						
	3.83	11.2	19	40.7	59.7	77	

CLAIMS:

CLMS(1)

We claim:

1. Adsorption material for the selective removal of Lp(a) lipoprotein, **LDL** cholesterol and/or vLDL cholesterol from aqueous liquids, said material consisting of:
a) porous glass **beads** as a solid carrier material, and

b) two or more different organic functional groups as ligands which are covalently bound via silanol groups present on their surface;
i) wherein a first ligand corresponds to formula I ##STR2## in which x and y denote integers from 1 to 5, and ii) wherein a second or third ligand is selected from the group consisting of: ligands corresponding to formula II,

--(CH.sub.2).sub.x --O--(CH.sub.2).sub.y --CH.sub.2 --OH (II)
in which x and y denote integers from 1 to 5, and ligands corresponding to formula III,

--(CH.sub.2).sub.x --O--(CH.sub.2).sub.y --CR.sub.1 R.sub.2 R.sub.3 (III)
in which R.sub.1 denotes a methoxy residue, R.sub.2 and R.sub.3 denote H or a methoxy residue, and x and y denote integers from 1 to 5, and wherein the material has no free silanol groups.

CLAIMS:

CLMS(7)

7. The adsorption material as claimed in claim 1, wherein the glass **beads** have a particle diameter of 60 to 500 .mu.m and a pore diameter of 50 to 350 nm.

CLAIMS:

CLMS(8)

8. A process for the removal of **LDL** cholesterol and/or vLDL cholesterol and/or Lp(a) lipoprotein from aqueous liquids, wherein the liquid is passed over the adsorption material of claim 1.

CLAIMS:

CLMS(10)

10. A method for the determination of the concentration of **LDL** cholesterol and/or VLDL cholesterol and/or Lp(a) lipoprotein in aqueous liquids, wherein
a) **LDL** cholesterol and vLDL cholesterol and Lp(a) lipoprotein are separated chromatographically with the aid of the adsorption material of claim 1; and
b) after elution from the adsorption material, the concentrations of **LDL** cholesterol and VLDL cholesterol and Lp(a) lipoprotein are determined.

CLAIMS:

CLMS(12)

12. A device for the extracorporeal removal of **LDL** cholesterol and/or vLDL cholesterol and/or Lp(a) lipoprotein from aqueous liquids, wherein the device consists of a cylindrical housing which is filled with the adsorption material of claim 1 and which is provided with covers at both ends which each have a central inflow or outflow pipe.

CLAIMS:

CLMS(18)

18. The device of claim 12, wherein the housing is integrated into a closed circulation in which the aqueous liquid, from which the **LDL**

cholesterol and/or vLDL cholesterol and/or Lp(a) lipoprotein are being removed, is circulated by means of a pump.

CLAIMS:

CLMS(20)

20. Adsorption material for the selective removal of Lp(a) lipoprotein, **LDL** cholesterol and/or vLDL cholesterol from aqueous liquids, said material consisting of:
a) porous glass **beads** as a solid carrier material, and
b) two or more different organic functional groups as ligands which are covalently bound via silanol groups present on their surface;
i) wherein a first ligand corresponds to formula I ##STR3## in which x and y denote integers from 1 to 5 and ii) a second ligand corresponds to formula II

--(CH.sub.2).sub.x --O--(CH.sub.2).sub.y --CH.sub.2 --OH (II)
in which x and y denote integers from 1 to 5, and wherein the material has no free silanol groups.

CLAIMS:

CLMS(23)

23. Adsorption material for the selective removal of Lp(a) lipoprotein, **LDL** cholesterol and/or vLDL cholesterol from aqueous liquids, said material consisting of:
a) porous glass **beads** as a solid carrier material; and
b) two or more different organic functional groups as ligands which are covalently bound via silanol groups present on their surface;
i) wherein a first ligand corresponds to formula I ##STR4## in which x and y denote integers from 1 to 5 and ii) a third ligand corresponds to formula III

--(CH.sub.2).sub.x --O--(CH.sub.2).sub.y --CR.sub.1 R.sub.2 R.sub.3 (III)
in which
R.sub.1 denotes a methoxy residue,
R.sub.2 and R.sub.3 denote H or a methoxy residue, and
x and y denote integers from 1 to 5, and wherein the material has no free silanol groups.

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